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What Is Claimed Is:

- 1. An oligonucleotide useful as a primer for inducing mutagenesis in a complementarity determining region (CDR) of an immunoglobulin light chain gene, said oligonucleotide having 3' and 5' termini and comprising:
- a) a nucleotide sequence at said 3' terminus capable of hybridizing to a first framework region of an immunoglobulin gene;
- b) a nucleotide sequence at said 5' terminus capable of hybridizing to a second framework region of an immunoglobulin gene; and
- c) a nucleotide sequence between said 3' and 5' termini according to the formula:

[NNK],

wherein N is independently any nucleotide, K is G or T, n is 3 to about 24, said 3' and 5' terminal nucleotide sequences having a length of about 6 to 50 nucleotides, or an oligonucleotide having a sequence complementary thereto.

- 2. The oligonucleotide of claim 1 wherein said 5' terminus has the nucleotide sequence 5'TATACTGTCAGCAGTAT-3' (SEQ ID NO 26) or 5'GATTTTGCAGTGTATTACTGTCAGCAGTAT-3' (SEQ ID NO 27), or an oligonucleotide having a sequence complementary thereto.
- 3. The oligonucleotide of claim 1 wherein said 3' terminus has the nucleotide sequence 5'ACTTTCGGCGGAGGGACCAAGGTGGAG-3' (SEQ ID NO 28) or 5'ACTTTCGGCGGAGGGACC-3' (SEQ ID NO 29), or an oligonucleotide having a sequence complementary thereto.
- 4. The oligonucleotide of claim 1 wherein n is 4, 5, 6, 10 or 16.

- The oligonucleotide of claim 1 wherein said immunoglobulin is human.
- The oligonucleptide of claim 1 wherein said CDR is CDR3.
- The oligonucleotide of claim 1 according to 7. the formula: 5'-GATTTTGCAGTGTATTACTGT [NNK] TOGCGGAGGGACCAAGGTGGAG-3' (SEQ ID NO 12), or an oligonucleotide having a sequence complementary thereto. \
- 8. An oligonucleotide useful as a primer for inducing mutagenesis in a complementarity determining region (CDR) of an immunoglobulin light chain gene, said oligonucleotide having 3' and 5' termini and comprising:
- a nucleotide sequence at said 3' a) terminus capable of hybridizing to a first framework region of an immunoglobulin gene;
- a nucleotide sequence at said 5' b) terminus capable of hybridizing to a second framework region of an immunoglobulin gene; and
- a nucleotide sequence between said 3' C) and 5' termini according to the formula:

[MNN],

wherein N is independently any nucleotide, M is A or C, n is 3 to about 24, said 3' and 5' terminal nucleotide sequences having a length of about 6 to 50 nucleotides, or an oligonucleotide having a sequence complementary thereto.

- The oligonuclectide of claim 8 wherein said 5' terminus has the nucleotide sequence 5'-GTTCCACCTTGGTCCCTTGGCCGAA-3'\(SEQ ID NO 30), or an oligonucleotide having a sequence complementary thereto.
- The oligonucleotide of claim 8 wherein said 10. 3' terminus has the nucleotide sequence 5'-

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ACAGTAGTACACTGCAAAATO 3 oligonucleotide having a thereto.

(SEQ ID NO 31), or an a sequence complementary

- 11. The oligonucleotide of claim 8 wherein n is 8, 10 or 16.
- 12. The oligonucleotide of claim 8 wherein said immunoglobulin is human.
- 13. The oligonucle of claim 8 wherein said CDR is CDR3.

14. A method for producing an antibody combining site in a polypeptide comprising inducing mutagenesis in a complementarity determining region (CDR) of an immunoglobulin light chain gene which comprises amplifying a CDR portion of the immunoglobulin gene by polymerase chain reaction (PCR) using a PCR primer oligonucleotide, said oligonucleotide having 3' and 5'

termini and comprising:

- a) a nucleotide sequence at said 3' terminus capable of hybridizing to a first framework region of an immunoglobulin gene;
- b) a nucleotide sequence at said 5' terminus capable of hybridizing to a second framework region of an immunoglobulin gene; and
- c) a nucleotide sequence between said 3' and 5' termini according to the formula:

[NNK],

wherein N is independently any nucleotide, K is G or T, and n is 3 to about 24, said 3' and 5' terminal nucleotide sequences having a length of about 6 to 50 nucleotides, or an oligonucleotide having a sequence complementary thereto.

15. The method of claim 14 wherein said 5' terminus has the nucleotide sequence 5'TATACTGTCAGCAGTAT-3' (SEQ ID NO 26) or 5'GATTTTGCAGTGTATTACTGTCAGCAGTAT-3' (SEQ ID NO 27), or

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an oligonucleotide having a sequence complementary thereto.

- The method of claim 14 wherein said 3' 16. terminus has the nucleotide sequence 5'-ACTTTCGGCGGAGGGACCAAGGTGGAG-3' (SEQ ID NO 28) or 5'-ACTTTCGGCGGAGGGACC-3' (SEQ ID NO 29), or an oligonucleotide having a sequence complementary thereto.
- 17. The method of claim 14 wherein n is 4, 5, 6, 10 or 16.
- 18. The method of claim 14 wherein said immunoglobulin is human.
- The method of claim 14 wherein said CDR is CDR3.
- 20. The method of claim 14 according to the formula: 5'-GATTTTGCAGTGTATTACTGT[NNK], TTCGGCGGAGGGACCAAGGTGGAG-3' (SEQ ID NO 12), or an oligonucleotide having a sequence complementary thereto.
- The method of claim 14 wherein said immunoglobulin light chain gene includes a sequence having the sequence characteristics of the light chain shown in SEQ\ID NO 2 or in SEQ ID NO 62.
- The method of claim 14 wherein said immunoglobulih light chain gene has the sequence characteristids of the light chain gene in ATCC Accession No. 75408.
- The method of claim 14 that further comprises the steps of:
- isolating the amplified CDR to form a library of mutagenized immunoglobulin light chain genes;
 - expressing the isolated library of b) mutagenized light chain genes in combination with one or more heavy chain genes to form a combinatorial

TSRI 409.1 antibody library of expressed heavy and light chain genes; and antibody library of expressed heavy and light chain

antibody library for the ability to bind a preselected genes; c) selecting ability to bind a preselected antibody library for the ability antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to bind a preselected antibody library for the ability to be a antigen. The method of claim 23 wherein said one of claim 24. chain genes. for producing an antibody combining an antibody combining an antibody combining an antibody combining an antibody. 25. A method for producing an antibody combining inducing mutagenesis of an apolypeptide comprising inducing (MAR) of an site in a polypeptide determining region site in a polypeptide comprising inducing matagenesis

site in a polypeptide determining which comprises

in a complementarity chain dene which comprises

in a complementaliant chain dene Immunoglobulin light chain of the immunoglobulin acres of the immunoglobulin a corporation (porp) weight a chain reaction (porp) weight applifying a chain reaction In a complementarity determining region which comprises immunoglobulin light chain gene which comprises immunoglobulin are remained to the complementarity of the complementarity of the comprises of the complementarity of the comprises of the complementarity of the complement antigen. heavy chain genes. amplifying a CDR portion of the immunoglobulin gene primer using a pCR primer having 3, and polymerase chain reaction of the immunoglobulin gene having 3, and polymerase chain said oligonucleor/de having 3, and and black said oligonucleor/de having 3, and and black said oligonucleor/de having 3, and and black said oligonucleor/de having 3, and and a said oligonucleor/de having 3, and and a said oligonucleor/de having 3, and a said oligonucleor/de Polymerase chain reaction (PCR) using a pck primer and 5' said oligonucleotide having 3' and 5' oligonucleotide. 5 a nucleotide sequence at said 3' framework

a nucleotide sequence at first framework
to a first framework
terminus capable of hybridizing
to a first framework
terminus capable of hybridizing
to a first framework 20 terminus capable of hybridizing to a second framework immunorionalin nene. termini and comprising: region of an immunoglobulin gene; an immunoglopulin gene; and between said 3' region of an immunoglobulin gene; 15 wherein N is independently any nucleotide, wis A or and si rerminal and 5' termini according to the formula: C. n is 3 to about 24, said 3 length of about 6 to 50 nucleotides. Or an olignnucleotides. wherein N is independently any nucleotide, M is and 5' terminal and 5' termina nucleotides or an oligonucleotide having a sequence ha the method of claim 25 wherein said 5' terminus has the nucleotide sequence 5'- 30', or an emantary grace commission as a march commission of an emantary grace commission as a march commission of a marriage control terminus has the nucleotide sequence 5'oligonucleotide having a sequence complementary complementary thereto. 25 30 thereto.

- 27. The method of claim 25 wherein said 3' terminus has the nucleotide sequence 5'-ACAGTAGTACACTGCAAAATC-3' (SEQ ID NO 31), or an oligonucleotide having a sequence complementary thereto.
- 28. The method of claim 25 wherein n is 8, 10 or 16.
- 29. The method of claim 25 wherein said immunoglobulin is human.
- 30. The method of claim 25 wherein said CDR is CDR3.

immunoglobulin light chain gene includes a sequence having the sequence characteristics of the light chain shown in SEQ ID NO 2 or in SEQ ID NO 62.

- 32. The method of claim 25 wherein said immunoglobulin light chain gene has the sequence characteristics of the light chain gene in ATCC Accession No. 75408.
- 33. The method of claim 25 that further comprises the steps of:
- a) isolating the amplified CDR to form a library of mutagenized immunoglobulin light chain genes;
- b) expressing the isolated library of mutagenized light thain genes in combination with one or more heavy chain genes to form a combinatorial antibody library of expressed heavy and light chain genes; and
- c) selecting species of said combinatorial antibody library for the ability to bind a preselected antigen.
- 34. The method of claim 33 wherein said one or more immunoglobulin heavy chain genes is a library of heavy chain genes.

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